BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

```
=> file caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   149.35     155.64

FILE 'CAPLUS' ENTERED AT 20:12:14 ON 29 JUL 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2003 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 29 Jul 2003  VOL 139 ISS 5
FILE LAST UPDATED: 28 Jul 2003  (20030728/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

=> s l4 and memantin?
          348 L4
          455 MEMANTIN?
L5          6 L4 AND MEMANTIN?

=> d l5 abs ibib kwic hitstr 1-6

L5   ANSWER 1 OF 6  CAPLUS  COPYRIGHT 2003 ACS on STN
AB   The invention provides compns. and methods for treating a human patient
     afflicted with a neuropsychiatric disorder.  Specifically, the invention
     provides for compns. and methods of modulating or antagonizing the
     activity of neuronal NMDA receptors, wherein such antagonistic activity is
     capable of modulating the glutamate induced excitatory response of the
     neurons, thereby inhibiting an excitotoxic effect, promoting a
     neurotrophic effect, and thereby providing a therapeutic effect that
     treats the neuropsychiatric disorder.  The NMDA antagonists of the
     invention include aminoadamantane derivs, e.g. memantine and
     nitromemantine.  Prepn. and biol. testing of adamantane derivs. of the
     invention are described.
ACCESSION NUMBER:        2002:449501  CAPLUS
DOCUMENT NUMBER:         137:28308
TITLE:                   Methods for treating neuropsychiatric disorders with
                         NMDA receptor antagonists
INVENTOR(S):             Lipton, Stuart M. D.
PATENT ASSIGNEE(S):      Neuromolecular Inc., USA
SOURCE:                  PCT Int. Appl., 67 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:           Patent
LANGUAGE:                English
```

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002045710	A1	20020613	WO 2001-US48516	20011207
WO 2002045710	C2	20030424		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2002029056	A5	20020618	AU 2002-29056 20011207

PRIORITY APPLN. INFO.: US 2000-254007P P 20001207
WO 2001-US48516 W 20011207

AB . . . thereby providing a therapeutic effect that treats the neuropsychiatric disorder. The NMDA antagonists of the invention include aminoadamantane derivs, e.g. **memantine** and nitromemantine. Prepn. and biol. testing of adamantane derivs. of the invention are described.

ST NMDA receptor antagonist neuropsychiatric disorder; aminoadamantane deriv prepn NMDA antagonist neuropsychiatric disorder; **memantine** nitromemantine NMDA antagonist neuropsychiatric disorder

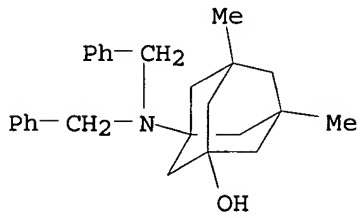
IT 19982-08-2, **Memantine** 19982-08-2D, **Memantine**, enantiomers and nitro derivs
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA antagonists for treating neuropsychiatric disorders)

IT 14670-98-5P 351329-87-8P 356572-01-5P 356572-03-7P 356572-08-2P 356572-10-6P 356572-12-8P **356572-15-1P** 356572-20-8P 356572-22-0P 356572-26-4P 356572-28-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; NMDA antagonists for treating neuropsychiatric disorders)

IT **356572-15-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and reaction; NMDA antagonists for treating neuropsychiatric disorders)

RN 356572-15-1 CAPLUS

CN Tricyclo[3.3.1.13,7]decan-1-ol, 3-[bis(phenylmethyl)amino]-5,7-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

AB We tested two approaches to overcoming resistance of influenza A viruses against adamantane derivs. First, adamantane derivs. that interfere with the ion channel function of the variant M2 protein of amantadine-resistant viruses may prevent drug resistance, if they are used in mixt. with amantadine. Second, amantadine acts on the M2 protein (at low concns.) and indirectly on the hemagglutinin (at concns. at least 100 times higher). Identifying and using a drug that reacted with both targets at the same concn. might reduce development of resistance, since, in this case, two mutations, one in each target protein would be necessary at once. Such a double mutation is assumed to be a rare event. We evaluated forty adamantane derivs. and two related compds. to det. whether they interfered with plaque formation by influenza A strains, including A/Singapore/1/57 (H2N2). Variants resistant to drugs that interfered at low concns. (.apprxeq.1 .mu.g/mL; e.g. amantadine) were cross-resistant with each other, but were sensitive to those agents effective at high concns. (8 .mu.g/mL; e.g. **memantine**). The former group of compds. act on the ion channel; the corresponding escape mutants tested had amino acid replacements at positions 27, 30 or 31 of the M2 protein. Hemagglutinin was the indirect target of the latter group of compds. Variants resistant to these agents lacked amino acid replacements within the ion channel of the M2 protein and the mutants tested had amino acid replacements in the hemagglutinin. Although we failed to identify compds. that interacted with the ion channel of amantadine-resistant variants and inhibited their replication, we were able to construct at least two compds. that interfered with both the ion channel and the hemagglutinin at about the same concn. After passage in the presence of these compds., we either failed to obtain any drug-resistant mutants or those obtained had amino acid replacements in the ion channel of the M2 protein and the hemagglutinin.

ACCESSION NUMBER: 1998:180033 CAPLUS
DOCUMENT NUMBER: 129:160
TITLE: How to overcome resistance of influenza A viruses against adamantane derivatives
AUTHOR(S): Scholtissek, C.; Quack, G.; Klenk, H. D.; Webster, R. G.
CORPORATE SOURCE: Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN, 38101, USA
SOURCE: Antiviral Research (1998), 37(2), 83-95
CODEN: ARSRDR; ISSN: 0166-3542
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

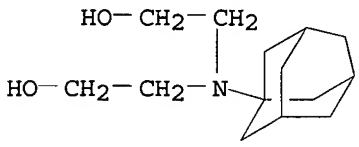
AB . . . e.g. amantadine) were cross-resistant with each other, but were sensitive to those agents effective at high concns. (8 .mu.g/mL; e.g. **memantine**). The former group of compds. act on the ion channel; the corresponding escape mutants tested had amino acid replacements at. . .

IT 281-23-2D, Adamantane, derivs. 669-51-2 768-94-5, Amantadine 3716-62-9 **3716-67-4** 3717-38-2 **3717-40-6** 3717-44-0 **3717-61-1** 3728-71-0 6240-07-9 10523-68-9 17768-41-1, Tricyclo[3.3.1.13,7]decane-1-methanamine 19982-07-1 19982-08-2, **Memantine** 22607-75-6, 4-Azatricyclo[4.3.1.13,8]undecan-5-one 28224-43-3 31897-98-0 38789-54-7 41031-30-5 51545-05-2 **54900-91-3** 54900-94-6 64310-42-5 80121-61-5 110916-45-5

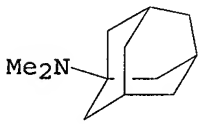
128487-55-8 134562-61-1 134562-70-2 171567-73-0 207406-28-8
207406-31-3 207406-32-4 207406-33-5 207406-34-6 207406-35-7
207406-36-8 207406-37-9 207406-38-0 207406-39-1 207406-40-4
207406-41-5 207406-42-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ion channel of M2 protein and hemagglutinin in overcoming resistance of influenza A viruses against adamantane derivs.)

IT **3716-67-4 3717-40-6 3717-61-1**
54900-91-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ion channel of M2 protein and hemagglutinin in overcoming resistance of influenza A viruses against adamantane derivs.)

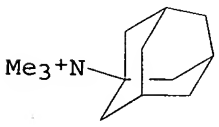
RN 3716-67-4 CAPLUS
CN Ethanol, 2,2'-(tricyclo[3.3.1.13,7]dec-1-ylimino)bis- (9CI) (CA INDEX NAME)



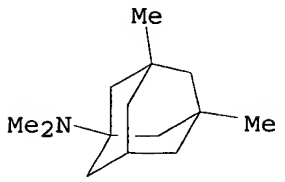
RN 3717-40-6 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 3717-61-1 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-aminium, N,N,N-trimethyl-, iodide (9CI) (CA INDEX NAME)



RN 54900-91-3 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N,3,5-tetramethyl-, hydrochloride (9CI) (CA INDEX NAME)



○ HCl

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

AB The amino-adamantane derivs. **memantine** (1-amino-3,5-dimethyladamantane) and amantadine (1-amino-adamantane) are relatively low affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists which have been used clin. in the treatment of dementia and Parkinson's disease resp. for several years without serious side effects. The aim of this study was to test whether **memantine**, amantadine and other low affinity uncompetitive NMDA receptor antagonists also have better therapeutic indexes than high affinity antagonists in preclin. models of epilepsy by assessing the potency, kinetics and voltage-dependency of open channel blockade for a series antagonists in vitro and comparing these effects to anticonvulsive and motor impairment activity in vivo. The compds. tested were **memantine**, amantadine, 14 other amino-adamantanes, (+)-MK-801, ketamine, dextrorphan, dextromethorphan and phencyclidine. The offset kinetics of open-channel blockade assessed with whole cell patch clamp recordings from cultured superior colliculus neurons were highly correlated to potency i.e. the less potent antagonists showed faster unblocking kinetics (Koff, r = 0.904). Although, onset kinetics as assessed by Kon were not correlated to potency (r = 0.023), .tau.on estd. at IC50 is perhaps a more meaningful measure of onset kinetics at equieffective concns. and was also well correlated to potency (r = - 0.863). All amino-adamantanes tested were strongly voltage-dependent. There was also a good correlation between the in vitro potencies of uncompetitive NMDA receptor antagonists assessed with patch clamp recordings and displacement of equil. [3H](+)-MK-801 binding and their in vivo activity against maximal electroshock (MES) and pentylenetetrazol (PTZ) induced tonic convulsions and NMDA-induced lethality in mice. **Memantine** and four other amino-adamantanes with somewhat lower potency and faster blocking kinetics had better therapeutic indexes (ED50 rotarod and traction reflex over ED50 in MES-induced convulsion; TI = 2-4) than substances with higher affinity such as ketamine, dextrorphan and (+)-MK-801 (TI < 2). However, amantadine and several other amino-adamantanes with lower potency than **memantine** actually had poorer therapeutic indexes (TI .ltoreq. 0.5) which may have been due to addnl. actions at other ion channels or receptors at the doses necessary to protect against seizures. In fact, ED50 in the MES test was neg.-correlated to therapeutic indexes (traction r = -0.790, rotarod r = -0.797) i.e. the less potent uncompetitive antagonists had worse therapeutic indexes. The data from the present study do not lend support to the idea that low affinity, open channel NMDA receptor blockers are also effective in models of epilepsy at doses having

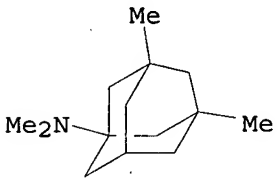
little effect on physiol. processes. It should be stressed that these data do not contradict the known therapeutic safety of **memantine** and amantadine in dementia and Parkinson's disease resp. Thus the good clin. profile of **memantine** in dementia has been attributed not only to its fast blocking/unblocking kinetics but also to its strong voltage-dependency. These biophys. properties may allow therapeutically-relevant concns. to block chronic, low level pathol. activation of NMDA receptors while leading their synaptic activation intact. Precisely these properties may also underlie the poor therapeutic indexes seen in the present study on antiepileptic activity due to the synaptic nature of both seizures and normal glutamatergic transmission.

ACCESSION NUMBER: 1995:908477 CAPLUS
DOCUMENT NUMBER: 124:21593
TITLE: Comparison of the potency, kinetics and voltage-dependency of a series of uncompetitive NMDA receptor antagonists in vitro with anticonvulsive and motor impairment activity in vivo
AUTHOR(S): Parsons, C. G.; Quack, G.; Bresink, I.; Baran, L.; Przegalinski, E.; Kostowski, W.; Krzascik, P.; Hartmann, S.; Danysz, W.
CORPORATE SOURCE: Department Pharmacology, Merz & Co., Frankfurt Main, D-60318, Germany
SOURCE: Neuropharmacology (1995), 34(10), 1239-58
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The amino-adamantane derivs. **memantine** (1-amino-3,5-dimethyladamantane) and amantadine (1-amino-adamantane) are relatively low affinity, uncompetitive N-methyl-D-aspartate (NMDA) receptor antagonists which have been used clin. in the. . . and Parkinson's disease resp. for several years without serious side effects. The aim of this study was to test whether **memantine**, amantadine and other low affinity uncompetitive NMDA receptor antagonists also have better therapeutic indexes than high affinity antagonists in preclin.. . . series antagonists in vitro and comparing these effects to anticonvulsive and motor impairment activity in vivo. The compds. tested were **memantine**, amantadine, 14 other amino-adamantanes, (+)-MK-801, ketamine, dextrorphan, dextromethorphan and phencyclidine. The offset kinetics of open-channel blockade assessed with whole cell. . . and their in vivo activity against maximal electroshock (MES) and pentylenetetrazol (PTZ) induced tonic convulsions and NMDA-induced lethality in mice. **Memantine** and four other amino-adamantanes with somewhat lower potency and faster blocking kinetics had better therapeutic indexes (ED50 rotarod and traction. . . affinity such as ketamine, dextrorphan and (+)-MK-801 (TI < 2). However, amantadine and several other amino-adamantanes with lower potency than **memantine** actually had poorer therapeutic indexes (TI .ltoreq. 0.5) which may have been due to addnl. actions at other ion channels. . . little effect on physiol. processes. It should be stressed that these data do not contradict the known therapeutic safety of **memantine** and amantadine in dementia and Parkinson's disease resp. Thus the good clin. profile of **memantine** in dementia has been attributed not only to its fast blocking/unblocking kinetics but also to its strong voltage-dependency. These biophys.. . .
IT 77-10-1, Phencyclidine 125-71-3, Dextromethorphan 125-73-5, Dextrorphan 768-94-5, Amantadine 6740-88-1, Ketamine 19982-08-2, **Memantine** 23264-83-7, Mrz 2/151 26482-53-1, Mrz 2/174

41100-49-6, Mrz 2/169 77086-22-7, (+)-MK-801 80121-60-4, Mrz 2/150
80904-86-5, Mrz 2/177 110894-15-0, Mrz 2/406 110916-46-6, Mrz 2/138
135295-60-2, Mrz 2/170 171567-73-0 171675-48-2, Mrz 2/372
171675-49-3, Mrz 2/153 171675-50-6, Mrz 2/457 171746-20-6, Mrz 2/247
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of the potency, kinetics and voltage-dependency of a series of uncompetitive NMDA receptor antagonists in vitro with anticonvulsive and motor impairment activity in vivo)

IT **135295-60-2**, Mrz 2/170
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparison of the potency, kinetics and voltage-dependency of a series of uncompetitive NMDA receptor antagonists in vitro with anticonvulsive and motor impairment activity in vivo)

RN 135295-60-2 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N,3,5-tetramethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN

AB The 1-aminoadamantanes **memantine** (1-amino-3,5-dimethyladamantane) and amantadine (1-aminoadamantane) are clin. used as antiparkinsonian, anti-spasticity, anti-dementia and antiviral drugs. The authors have tested 1-aminoadamantane derivs. including **memantine** and amantadine for their ability to compete with [3H](+)-pentazocine in homogenates of post-mortem human frontal cortex. The Ki values ranged from 0.237 .+-. 0.019 .mu.M for 1-N-dimethylamino-3,5-dimethyladamantane to 20.25 .+-. 16.48 .mu.M for amantadine. The Ki values of **memantine** was 19.98 .+-. 3.08 .mu.M and was thus very similar to that of amantadine. **Memantine**, at therapeutic concns., probably does not interact with the .sigma. binding site. Amantadine, at therapeutic concns., probably binds both to the .sigma. site and to the phencyclidine (PCP) binding site of the N-methyl-D-aspartate (NMDA) receptor.

ACCESSION NUMBER: 1994:95468 CAPLUS
DOCUMENT NUMBER: 120:95468
TITLE: Affinity of 1-aminoadamantanes for the .sigma. binding site in post-mortem human frontal cortex
AUTHOR(S): Kornhuber, J.; Schoppmeyer, K.; Riederer, P.
CORPORATE SOURCE: Dep. Psychiatry, Univ. Wuerzburg, Wuerzburg, Germany
SOURCE: Neuroscience Letters (1993), 163(2), 129-31
CODEN: NELED5; ISSN: 0304-3940
DOCUMENT TYPE: Journal
LANGUAGE: English

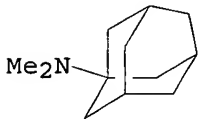
AB The 1-aminoadamantanes **memantine** (1-amino-3,5-dimethyladamantane) and amantadine (1-aminoadamantane) are clin. used as antiparkinsonian, anti-spasticity, anti-dementia and antiviral drugs. The authors have tested 1-aminoadamantane derivs. including **memantine**

and amantadine for their ability to compete with [3H](+)-pentazocine in homogenates of post-mortem human frontal cortex. The Ki values ranged from 0.237 .+-. 0.019 .mu.M for 1-N-dimethylamino-3,5-dimethyladamantane to 20.25 .+-. 16.48 .mu.M for amantadine. The Ki values of **memantine** was 19.98 .+-. 3.08 .mu.M and was thus very similar to that of amantadine. **Memantine**, at therapeutic concns., probably does not interact with the .sigma. binding site. Amantadine, at therapeutic concns., probably binds both to. . .

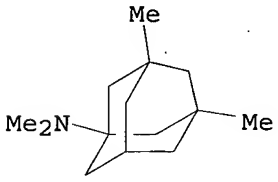
IT 768-94-5, Amantadine 3717-38-2 **3717-40-6** 19982-08-2, **Memantine** 41100-49-6 61051-37-4 134562-70-2 **135295-60-2**
RL: BIOL (Biological study)
(.sigma. receptors of brain frontal cortex of humans binding by, pharmacol. in relation to)

IT **3717-40-6 135295-60-2**
RL: BIOL (Biological study)
(.sigma. receptors of brain frontal cortex of humans binding by, pharmacol. in relation to)

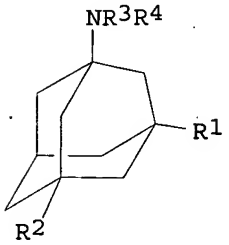
RN 3717-40-6 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 135295-60-2 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N,3,5-tetramethyl- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

10/016,850

AB A series of 1-aminoadamantanes (I, R1 = H, alkyl, Ph; R2 and R3 = H, Me or Et; R4 = H or Me), including amantadine I (R1-R4 = H) and **memantine** I (R1 = R2 = Me; R3 = R4 = H), were tested for their ability to compete with [3H]MK-801 binding in membrane homogenates of postmortem human frontal cortex. The most potent substance (1-amino-3,5-diethyladamantane) had a Ki- of 0.19 .mu.M while the weakest substance [(1-(methylamino)adamantane] had a Ki- of 21.72 .mu.M. The Ki- of amantadine was 10.50 .mu.M. In agreement with the earlier investigation, the Ki- of **memantine** was 0.54 .mu.M. Thus, 1-aminoadamantanes, in general, may produce their pharmacol. effects through an interaction with the NMDA-receptor-gated ion channel. The displacement of [3H]MK-801 binding may provide the basis to predict the antiparkinsonian and antispastic activity of novel substituted 1-aminoadamantanes and possibly of other drugs.

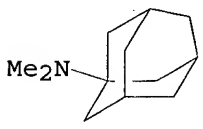
ACCESSION NUMBER: 1991:464578 CAPLUS
DOCUMENT NUMBER: 115:64578
TITLE: Effects of the 1-amino-adamantanes at the MK-801-binding site of the NMDA-receptor-gated ion channel: a human postmortem brain study
AUTHOR(S): Kornhuber, Johannes; Bormann, Joachim; Huebers, Marianne; Rusche, Kristin; Riederer, Peter
CORPORATE SOURCE: Dep. Psychiatry, Univ. Wuerzburg, Wuerzburg, D-8700, Germany
SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1991), 206(4), 297-300
CODEN: EJPPET; ISSN: 0922-4106
DOCUMENT TYPE: Journal
LANGUAGE: English

AB . . . R2 and R3 = H, Me or Et; R4 = H or Me), including amantadine I (R1-R4 = H) and **memantine** I (R1 = R2 = Me; R3 = R4 = H), were tested for their ability to compete with [3H]MK-801. . . Ki- of 21.72 .mu.M. The Ki- of amantadine was 10.50 .mu.M. In agreement with the earlier investigation, the Ki- of **memantine** was 0.54 .mu.M. Thus, 1-aminoadamantanes, in general, may produce their pharmacol. effects through an interaction with the NMDA-receptor-gated ion channel.. . .

IT 768-94-5, Amantadine 3717-38-2 **3717-40-6** 19982-08-2, **Memantine** 41100-45-2 41100-49-6 61051-37-4 80121-60-4 80904-86-5 134562-70-2 135295-59-9 **135295-60-2**
RL: BIOL (Biological study)
(methylaspartate receptor binding inhibition by, in brain of humans)

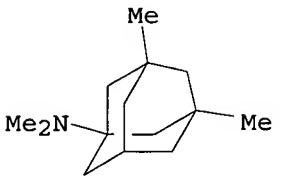
IT **3717-40-6 135295-60-2**
RL: BIOL (Biological study)
(methylaspartate receptor binding inhibition by, in brain of humans)

RN 3717-40-6 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N-dimethyl- (9CI) (CA INDEX NAME)

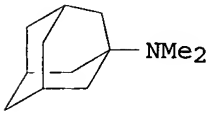


RN 135295-60-2 CAPLUS
CN Tricyclo[3.3.1.13,7]decan-1-amine, N,N,3,5-tetramethyl- (9CI) (CA INDEX NAME)

Delacroix



L5 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2003 ACS on STN
GI



I

AB **Memantine** (I) [**3717-40-6**] (10-4M) added to cultures of rat sensory nerve fibers decreased the amplitude of the summation action potential without affecting the resting potential, increased membrane resistance, and depressed the repetitive activity caused by depolarizing rectangular currents. I also decreased membrane conductance of Na+, K+, and Cl-.

ACCESSION NUMBER: 1977:527114 CAPLUS
DOCUMENT NUMBER: 87:127114
TITLE: The effect of **memantine** on membranes of sensory nerve fibers
AUTHOR(S): Grossmann, W.; Jurna, I.
CORPORATE SOURCE: Neurol. Klin., Tech. Univ. Muenchen, Munich, Fed. Rep. Ger.
SOURCE: Arzneimittel-Forschung (1977), 27(7), 1483-7
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German

TI The effect of **memantine** on membranes of sensory nerve fibers
AB **Memantine** (I) [**3717-40-6**] (10-4M) added to cultures of rat sensory nerve fibers decreased the amplitude of the summation action potential without affecting the. . .
ST **memantine** sensory nerve membrane
IT Cell membrane
(of sensory nerve, **memantine** effect on)
IT Nerve
(sensory, **memantine** effect on)
IT 7440-09-7, biological studies 7440-23-5, biological studies 16887-00-6, biological studies
RL: BIOL (Biological study)
(transport of, by cell membrane of sensory nerve, **memantine** effect on)

```
=> d his

     (FILE 'HOME' ENTERED AT 19:52:16 ON 29 JUL 2003)

     FILE 'REGISTRY' ENTERED AT 19:54:56 ON 29 JUL 2003
L1             STRUCTURE UPLOADED

     FILE 'STNGUIDE' ENTERED AT 20:01:31 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:09:38 ON 29 JUL 2003
L2             STRUCTURE UPLOADED
L3           50 S L2 SSS SAM
L4         1127 S L2 SSS FULL

     FILE 'CAPLUS' ENTERED AT 20:12:14 ON 29 JUL 2003
L5            6 S L4 AND MEMANTIN?

     FILE 'STNGUIDE' ENTERED AT 20:19:34 ON 29 JUL 2003

     FILE 'CAPLUS' ENTERED AT 20:34:52 ON 29 JUL 2003
L6            0 S L5 AND ADRENERGIC?
L7          348 S L4
L8            0 S L7 AND CONJUGAT? AND (ACTIVE(2A)AGENT? OR DRUG?)
L9           10 S L7 AND (CONJUGAT? OR LINKER? OR COVALENT)

     FILE 'STNGUIDE' ENTERED AT 20:41:12 ON 29 JUL 2003

     FILE 'STNGUIDE' ENTERED AT 20:44:19 ON 29 JUL 2003

     FILE 'STNGUIDE' ENTERED AT 20:45:52 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:47:20 ON 29 JUL 2003
L10            STRUCTURE UPLOADED
L11          50 S L10 SSS SAM
L12        1127 S L10 SSS FULL

     FILE 'STNGUIDE' ENTERED AT 20:49:12 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:56:22 ON 29 JUL 2003
L13            STRUCTURE UPLOADED
L14          47 S L13 SSS SAM
L15        1036 S L13 SSS FULL

     FILE 'CAPLUS' ENTERED AT 20:57:31 ON 29 JUL 2003

=>
```

```
=> d his

     (FILE 'HOME' ENTERED AT 19:52:16 ON 29 JUL 2003)

     FILE 'REGISTRY' ENTERED AT 19:54:56 ON 29 JUL 2003
L1             STRUCTURE UPLOADED

     FILE 'STNGUIDE' ENTERED AT 20:01:31 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:09:38 ON 29 JUL 2003
L2             STRUCTURE UPLOADED
L3           50 S L2 SSS SAM
L4         1127 S L2 SSS FULL

     FILE 'CAPLUS' ENTERED AT 20:12:14 ON 29 JUL 2003
L5            6 S L4 AND MEMANTIN?

     FILE 'STNGUIDE' ENTERED AT 20:19:34 ON 29 JUL 2003

     FILE 'CAPLUS' ENTERED AT 20:34:52 ON 29 JUL 2003
L6            0 S L5 AND ADRENERGIC?
L7          348 S L4
L8            0 S L7 AND CONJUGAT? AND (ACTIVE(2A)AGENT? OR DRUG?)
L9           10 S L7 AND (CONJUGAT? OR LINKER? OR COVALENT)

     FILE 'STNGUIDE' ENTERED AT 20:41:12 ON 29 JUL 2003

     FILE 'STNGUIDE' ENTERED AT 20:44:19 ON 29 JUL 2003

     FILE 'STNGUIDE' ENTERED AT 20:45:52 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:47:20 ON 29 JUL 2003
L10            STRUCTURE UPLOADED
L11          50 S L10 SSS SAM
L12        1127 S L10 SSS FULL

     FILE 'STNGUIDE' ENTERED AT 20:49:12 ON 29 JUL 2003

     FILE 'REGISTRY' ENTERED AT 20:56:22 ON 29 JUL 2003
L13            STRUCTURE UPLOADED
L14          47 S L13 SSS SAM
L15        1036 S L13 SSS FULL

     FILE 'CAPLUS' ENTERED AT 20:57:31 ON 29 JUL 2003
L16           0 S (L12 OR L15) AND (LINKER? OR CONJUGAT?) AND ADRENERGIC?
L17           0 S (L12 OR L15) AND PHARMACEUTICAL?(P)COMPOSITION?
L18         348 S (L12 OR L15)

     FILE 'REGISTRY' ENTERED AT 21:02:08 ON 29 JUL 2003
               E AMANTADINE/CN
L19           1 S E3

     FILE 'CAPLUS' ENTERED AT 21:04:49 ON 29 JUL 2003

=> s (l12 or l15) and (therapeutic? or drug or active(2a)agent) and (link? or
covalent? or conjugat?)
           348 L12
```

```
          318 L15
       167088 THERAPEUTIC?
       485882 DRUG
       788329 ACTIVE
       648969 AGENT
        11775 ACTIVE(2A)AGENT
       364486 LINK?
        81277 COVALENT?
       185843 CONJUGAT?
L20         0 (L12 OR L15) AND (THERAPEUTIC? OR DRUG OR ACTIVE(2A)AGENT) AND
              (LINK? OR COVALENT? OR CONJUGAT?)

=>
```